General

Guideline Title

ACR Appropriateness Criteria® radiologic management of thoracic nodules and masses.

Bibliographic Source(s)

English BS, Ray CE Jr, Chang JY, Crabtree TD, Gaba RC, Gipson MG, Iannettoni MD, Kouri BE, Marshalleck FE, Mohammed TL, Pinchot JW, Saleh AG, Willers H, Hohenwalter EJ, Expert Panel on Interventional Radiology. ACR Appropriateness CriteriaÂ® radiologic management of thoracic nodules and masses. Reston (VA): American College of Radiology (ACR); 2015. 14 p. [64 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Ray CE Jr, English B, Funaki BS, Burke CT, Fidelman N, Ginsburg ME, Kinney TB, Kostelic JK, Kouri BE, Lorenz JM, Nair AV, Nemcek AA Jr, Owens CA, Saleh AG, Vatakencherry G, Mohammed TH, Expert Panel on Interventional Radiology. ACR Appropriateness Criteria® radiologic management of thoracic nodules and masses. [online publication]. Reston (VA): American College of Radiology (ACR); 2011. 7 p. [39 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Radiologic Management of Thoracic Nodules and Masses

Variant 1: Middle-aged patient (35–60 years old) with an incidental 1.5-cm lung nodule. The lesion was smooth. No associated adenopathy. No known risk factors for lung cancer.

Treatment/Procedure	Rating	Comments
Percutaneous lung biopsy	7	If the patient has significant risk factors, biopsy would be even more indicated.
FDG-PET/CT whole body	7	
Follow-up imaging only	6	The size of the nodule is disconcerting, regardless of the other characteristics.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Treatment/Procedure	Rating	Comments
Surgical lung biopsy/resection	3	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: Middle-aged patient (35–60 years old) who had a CT pulmonary angiogram that was negative for pulmonary embolism but that demonstrated an incidental 1.5-cm lung nodule. The lesion was smooth. No associated adenopathy. Patient has a 70 pack/year smoking history and evidence of significant COPD on chest CT.

Treatment/Procedure	Rating	Comments
Percutaneous lung biopsy	8	
FDG-PET/CT whole body	8	
Surgical lung biopsy/resection	5	
Follow-up imaging only	2	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: Middle-aged patient (35–60 years old) with a newly diagnosed colon carcinoma. Three pulmonary nodules, ranging up to 2 cm in diameter, noted on staging CT of the chest. At least one of the lesions demonstrates a lobulated appearance.

Treatment/Procedure	Rating	Comments
Percutaneous lung biopsy	8	
FDG-PET/CT whole body	8	
Surgical lung biopsy/resection	3	This procedure is typically reserved for patients in whom percutaneous biopsy cannot be performed, or in patients with a negative percutaneous biopsy.
Follow-up imaging only	3	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: Young adult patient (20–35 years old) with 1.0-cm smooth-walled noncalcified lung nodule seen on CT after minor motor vehicle trauma. No known risk factors for lung cancer.

Treatment/Procedure	Rating	Comments
Follow-up imaging only	8	
Percutaneous lung biopsy	3	
FDG-PET/CT whole body	3	
Surgical lung biopsy/resection	2	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: Middle-aged patient (35–60 years old) with persistent 1.5-cm ground glass nodule noted on an initial CT scan and a follow-up 3-month CT scan. No smoking history and no recent respiratory infection.

Treatment/Procedure	Rating	Comments
Percutaneous lung biopsy	7	
Surgical lung biopsy/resection	6	Biopsy depends on local percutaneous expertise. Surgical resection may be performed following percutaneous biopsy.
FDG-PET/CT whole body	5	Bronchoalveolar carcinoma is often PET negative.
Follow-up imaging only	5	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 6: Elderly patient (>80 years old) with multifocal <2-cm pure ground-glass opacities (no solid component) after chest CT recommended from an abnormal coronary CT examination. No smoking history and no recent respiratory infection.

Treatment/Procedure	Rating	Comments
Follow-up imaging only	7	Ground-glass nodules typically have a slow growth rate, and a short interim follow-up study may show nodule resolution.
Percutaneous lung biopsy	4	This procedure is performed depending on the clinical functional status of the patient. This procedure may be acceptable, but generally imaging is done first. This procedure is reserved for persistent or growing ground-glass nodules.
Conservative management (do nothing)	4	Conservative management can be used if the patient will not have therapy. All of these can change over time with more data determining the efficacy of tumor-directed therapy (i.e., epidermal growth factor receptor inhibitors).
FDG-PET/CT whole body	3	FDG does not significantly accumulate in bronchoalveolar carcinoma, well-differentiated adenocarcinomas, and carcinoid tumors.
Surgical lung biopsy/resection	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 7: Middle-aged patient (35–60 years old) with a 2-cm smooth-walled lung nodule containing fatty elements by Hounsfield attenuation noted on CT. No prior imaging or risk factors for lung cancer.

Treatment/Procedure	Rating	Comments
Follow-up imaging only	6	Radiography or CT may be appropriate. For a likely hamartoma, confirm with repeat imaging. This procedure is recommended with a very low probability of cancer by pulmonary nodule calculators.
Conservative management (do nothing)	6	The patient should probably have at least 1 follow-up imaging study.
Percutaneous lung biopsy	2	Hamartomas do not usually require biopsy.
Surgical lung biopsy/resection	2	
FDG-PET/CT whole body	2	No additional imaging is needed. CT is diagnostic.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 8: Middle-aged patient (35–60 years old) with known multiple pulmonary nodules from metastatic cancer. All lesions but 1 have regressed on the current chemotherapy regimen.

Treatment/Procedure	Rating	Comments
Percutaneous lung biopsy	7	Sampling is important for mutational testing versus second primary. This procedure is particularly important if results will change therapy. This depends on the location of the lesion and its accessibility by percutaneous techniques. Sampling of nonresponding nodule is useful for mutational genetic testing.
Bronchoscopic biopsy (repeat biopsy)	6	Sampling is important for mutational testing versus second primary. This procedure is recommended only if lesion is adjacent to airway. Traditional transbronchial biopsy historically has a very low yield, but image-guided TBNA will have much better results (i.e., EBUS). This procedure is recommended if lesion is amenable to traditional or navigational bronchoscopic biopsy.
FDG-PET/CT whole body	6	This procedure may be appropriate to exclude disease elsewhere. This procedure is unlikely to change management. PET/CT is not helpful in differentiating between primary lung cancer and metastases. FDG-PET may be helpful in identifying nonpulmonary occult metastatic disease.
Surgical lung biopsy/resection	5	Sampling is important for mutational testing versus second primary. This procedure is recommended if lesion is inaccessible by percutaneous or bronchoscopic biopsy. Surgical biopsy may be important if there is uncertainty regarding the diagnosis of the lung lesions, if more tissue is needed to perform molecular testing, or if the patient is a candidate for curative resection, depending on the number of lesions.
Follow-up imaging only	5	This procedure may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
Conservative management (do nothing)	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 9: Elderly patient (>60 years old) with a positive purified protein derivative (tuberculin) test and abnormal chest radiograph. On CT scanning, bulky (up to 3 cm) mediastinal adenopathy is noted throughout the mediastinum (pretracheal, subcarinal, aortopulmonary window). The nodes do not demonstrate calcifications or necrosis. No associated pulmonary nodules.

Treatment/Procedure	Rating	Comments
Endoscopic/bronchoscopic biopsy	8	
Percutaneous mediastinal biopsy	5	Consider this procedure if bronchoscopic biopsy fails, and the mediastinal biopsy can be safely performed percutaneously.
Surgical mediastinal biopsy/resection	4	This procedure might be appropriate, depending on local percutaneous/bronchoscopic biopsy expertise and accessibility of the nodes by nonsurgical approaches.
Follow-up imaging only	2	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 10: Elderly patient (>60 years old) with a long (>30 pack/year) smoking history meeting criteria for low-dose screening CT (LDCT).

LDCT demonstrates a 2-cm pulmonary nodule in the lingula. There is mediastinal adenopathy (up to 2 cm) in the pretracheal and subcarinal regions as well as left perihilar (up to 2 cm) adenopathy.

Treatment/Procedure	Rating	Comments
Endoscopic/bronchoscopic mediastinal biopsy	8	This procedure depends on local expertise.
FDG-PET/CT whole body	8	
Percutaneous lung biopsy	7	
Percutaneous mediastinal biopsy	6	This procedure depends on local expertise and accessibility of the nodes by percutaneous approach.
Surgical pulmonary nodule biopsy/resection	3	
Follow-up imaging only	2	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 11: Middle-aged patient (35–60 years old) with shortness of breath presenting with bilateral hilar adenopathy measuring up to 2 cm, enlarging on serial 3-month imaging. Recent nondiagnostic bronchoscopic biopsy via TBNA. No intraparenchymal pulmonary nodules.

Treatment/Procedure	Rating	Comments
Bronchoscopic biopsy (repeat biopsy)	7	TBNA is operator dependent. Usually yield is increased with EBUS guidance. This procedure is recommended unless bronchoscopists think there is a reason the first biopsy was inadequate. This depends on the original bronchoscopic technique. Traditional transbronchial biopsy historically has a very low yield, but image-guided TBNA will have much better results (i.e., EBUS).
Follow-up imaging only	5	This procedure may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
FDG-PET/CT whole body	5	This procedure is mostly used for staging once the diagnosis is made or if there is a concern for systemic malignancy (extrathoracic neoplasm or lymphoma). This procedure is useful for staging of presumed malignancy.
Surgical lung biopsy/resection	4	This procedure is reserved for nondiagnostic bronchoscopic and percutaneous sampling.
Percutaneous lymph node biopsy	3	This procedure depends on anatomic location. This is almost never necessary for true hilar lymphadenopathy. This procedure is associated with increased pneumothorax risk for hilar biopsies.
Conservative management (do nothing)	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 12: Middle-aged patient (35–60 years old) presenting with a 3-cm lobular mass involving the left pleura associated with rib erosion.

Treatment/Procedure	Rating	Comments
Percutaneous lung biopsy	8	
FDG-PET/CT whole body	8	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Treatment/Procedure	Rating	Comments
Surgical pleural biopsy/resection	5	This procedure depends on accessibility by percutaneous approach. Surgical biopsy may be appropriate; however, resection is not likely possible.
Follow-up imaging only	1	
Conservative management (do nothing)	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

Lung cancer causes more deaths than the next 3 most common cancers combined (colon, breast, and prostate). An estimated 162,460 deaths from lung cancer occur in the United States each year, and the incidence of the disease is rising. The diagnosis of lung cancer carries a very poor prognosis: the expected 5-year survival rate for all patients in whom lung cancer is diagnosed is 15.5% (compared to 64.8% for colon, 89% for breast cancer and 99.9% for prostate cancer). Early diagnosis is vital and significantly improves survival rates. The 5-year survival rate approaches 50% in patients in whom the disease is detected when still localized and 70% for stage IA lung cancer. However, only about 1 in 4 lung cancer cases is diagnosed at an early stage.

Metastatic disease to the lungs can occur with virtually any primary malignancy. Diagnosis of such metastases allows for appropriate treatment and prognostication of patients with the disease. Although diffuse metastatic disease to the lungs typically mandates systemic treatment such as intravenous chemotherapy, some primary tumors such as sarcomas may metastasize solely to the lungs, and surgical resection may be curative.

Cases in which lung cancer is diagnosed at an early stage are typically asymptomatic, further delaying diagnosis. Solitary pulmonary nodules represent the most typical radiographic presentation of early lung cancer, and multiple pulmonary nodules may be the first sign of malignancy in a patient without a prior diagnosis. Biopsy of pulmonary nodules therefore allows for a tissue diagnosis of malignancy and, in some cases, staging of the primary tumor. Diagnosis by less invasive means may also preclude more invasive surgical procedures performed for diagnosis; this is particularly important in this high-risk patient population. For example, findings from positron emission tomography/computed tomography (PET/CT) have been shown to reduce the number of futile thoracotomies and the total number of thoracotomies.

Two recent studies have demonstrated the importance of radiologic imaging and lung cancer screening. The National Lung Cancer Screening Trial assessed whether lung cancer–related mortality could be decreased by having high-risk patients undergo 3 annual screenings with low-dose helical CT. Results from this study demonstrated that, when compared to chest radiography, screening with low-dose CT resulted in a decrease in the number of advanced-stage lung cancers while concurrently resulting in an increase in the number of early lung cancers. There was a 20% reduction in lung cancer mortality from the low-dose CT screening arm compared to chest radiography screening, and there was a 7% reduction in all-cause mortality. The second study evaluated the likelihood of malignancy based on predictive values of specific patient and nodule characteristics noted on screening low-dose CT. Results from this study demonstrated multiple patient and nodule characteristics that significantly increased the likelihood of malignancy, even for very small (<10 mm) pulmonary nodules.

Although these studies and others have demonstrated the ability of low-dose CT to identify early-stage malignancy in high-risk patients, concern has been raised about both the radiation exposure to the public with aggressive and widespread screening protocols as well as the low yield of screening protocols. In 1 large study from Italy (ITALUNG), a yield of only 2.0% for malignancy was noted in patients exposed to up to 4 annual screening CT scans.

It is important to note the demographic referenced as high risk for lung cancer. The Center for Medicare and Medicaid Services currently defines this high-risk population as individuals 55–74 years of age with a smoking history of at least 30 years who are either current smokers or have quit within the last 15 years.

Due to the nature of this document, its discussion of biopsies centers on percutaneous approaches. Since percutaneous biopsies are now typically considered a first-line procedure, there is a severe paucity of recent literature directly comparing percutaneous to other approaches (e.g., surgical, video-assisted thoracoscopy, or bronchoscopy with or without fluoroscopic or endobronchial/endoscopic ultrasound [EBUS] guidance). The reader should keep these other approaches in mind, and on a case-by-case basis based on anatomy and clinical presentation should determine whether or not nonpercutaneous approaches should be seriously considered.

Discussion by Variant

Variants 1 through 8: Pulmonary Nodules

Most biopsies in the thorax will be performed for pulmonary nodules. These nodules may be solitary or multiple; in the latter case, metastatic disease or an infectious etiology is more likely than a primary lung cancer. Initial clinical evaluation, including known risk factors for lung cancer, is necessary before biopsy is attempted. There are several published guidelines for the management of small pulmonary nodules detected on CT scans, the most widely cited of which is supported by the Fleischner Society. A new reporting and management lexicon developed in 2014 by the American College of Radiology serves as a quality assurance tool designed to standardize lung cancer CT screening reporting and management recommendations. This lung nodule management tool is referenced on the ACR Web site: http://www.acr.org/Quality-Safety/Resources/LungRADS .

Many nonradiologists use "pulmonary nodule calculators" to estimate the pretest probability of malignancy for any given solitary pulmonary nodule. By inputting several clinical and radiologic risk factors that increase the likelihood of malignancy (e.g., age, smoking history, and size and morphology of the nodule), a calculation is performed that gives the probability of malignancy for a patient presenting with a solitary pulmonary nodule. The American College of Chest Physicians recommends the use of pulmonary nodule calculators when determining the diagnostic and/or treatment algorithm to be undertaken for patients presenting with solitary pulmonary nodules. These calculators are widely available on the Internet.

There is a distinct paucity of evidence in the literature directly comparing biopsy techniques across multiple specialties. Methods by which biopsies may be obtained include percutaneous biopsy with imaging guidance, mediastinoscopy with biopsy, bronchoscopy-guided transbronchial biopsy, video-assisted thoracoscopy, endoscopic ultrasound (US) transesophageal biopsy, or open surgical biopsy. The location of the nodule (e.g., subpleural, paramediastinal, subcarinal, endobronchial) significantly affects the likelihood of success of one form of biopsy compared to another. Recent evidence suggests that adjustment of intraprocedural CT scanning techniques can significantly decrease the amount of radiation exposure during biopsies.

Patients in whom biopsies are performed are often considered to be at high risk for complications from the procedure. These risks (e.g., pneumothorax, bleeding, and bronchopleural fistula) are largely due to the poor underlying pulmonary reserve and high incidence of chronic obstructive pulmonary disease (COPD) in this patient population. Patients should be counseled before the procedure regarding the significant risks associated with their biopsy.

In addition to problems associated with a relatively high-risk patient population, percutaneous biopsies of pulmonary nodules may be difficult to perform technically. Patients may often have difficulty suspending respirations or may take variable volume breaths, resulting in the target lesion moving in and out of the biopsy plane. Lesions may also be very small or central (deep) in location, making needle placement challenging. For these reasons and others, the failure rate of lung biopsies is relatively high. The Society of Interventional Radiology guidelines for lung biopsy specify that an 85% success rate is acceptable.

Characteristics of pulmonary nodules affect the likelihood of malignancy. Morphologic characteristics, such as smooth and well-defined margins and diffuse or central nodular calcifications favor benign etiology. Although persistent ground-glass and mixed ground-glass density nodules have traditionally been thought to have a high rate of malignancy, recent evidence suggests that the slow progression of such nodules may indicate that active surveillance can be a reasonable approach to this patient population. The likelihood of cancer diagnosis increases with the size of the pulmonary nodule, regardless of solid or ground-glass density. Nodules >3 cm in diameter are considered pulmonary malignancies until proven otherwise. Other characteristics, such as growth rate, dynamic changes on contrast-enhanced helical CT, and uptake of fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) during PET imaging may help in distinguishing benign from malignant lesions.

A recent report demonstrates that the diameter of solid tumor size and maximum activity on PET demonstrate a greater predictive value for high-grade malignancies than the normally measured whole tumor size. Although the demonstration of certain characteristics with cross-sectional imaging has improved the likelihood of malignancy, CT has still not replaced biopsy as the definitive examination of choice. One recent study directly comparing CT findings with biopsy results (in 129 patients already considered to be high risk for malignancy, given their imaging findings) demonstrated a CT sensitivity of 95% and positive predictive value of 83% but also reported only 43% specificity and a 75% negative predictive value.

FDG is accumulated in malignant nodules. Benign lesions such as hamartomas and inflammatory nodules do not significantly accumulate FDG. Thus, PET is a valuable tool in evaluation of indeterminate lesions. In one meta-analysis of 1,474 pulmonary nodules, PET was 97% sensitive and 78% specific. It is important to recognize the limitations of PET. It is best used in patients with nodules >0.8 mm in diameter, as smaller nodules may result in a false-negative study. False-negative scans may also occur in cancer presenting as a predominant ground-glass opacity and with malignancies such as well-differentiated adenocarcinomas, bronchoalveolar cell carcinomas, and carcinoid tumors. False-positive lesions may result in patients with tuberculosis, fungal infections, or sarcoidosis. Although helpful in determining the FDG uptake and metabolic activity in pulmonary nodules, PET remains relatively inaccurate (particularly with regards to specificity) and therefore has limited use in the initial diagnosis of pulmonary malignancy. Once a tissue diagnosis is made, PET is the standard for initial staging before treatment and may prove to have a significant role in

pulmonary nodules post-treatment.

Transthoracic needle aspiration and biopsy are the mainstays for obtaining tissue for histopathologic diagnosis of pulmonary nodules, and they usually provide adequate tissue quantity for biochemical analysis. Endoscopic US-guided procedures allow only fine-needle aspiration (FNA) of individual cells, usually sufficient for staging purposes. However, recent advances in targeted cancer pharmacotherapy based on genetics of specific tumors may require a greater quantity of tissue and require more core biopsy specimens. Several technical measures may increase the yield or decrease the risk of percutaneous biopsies:

1. Preselecting patients with nodules having high potential for malignancy.
2. Providing on-site analysis of the specimen, rather than placing the specimen in fixative for later analysis, allows for higher diagnostic accuracy.
3. Performing both FNA and core biopsies of the same lesion has been shown to increase yield over FNA alone, particularly in the diagnosis of benign nodules.
4. Using a steeper angle of the biopsy needle and placing the patient prone may decrease the risk of pneumothorax.
5. Using a 19-gauge or smaller needle.

Percutaneous biopsy is limited in its ability to obtain a specific diagnosis of a benign pulmonary process, and yields of ≤50% are expected. Performing both core biopsies and FNA of benign lesions significantly increases the diagnostic yield. In addition, some investigators have suggested that multiple larger biopsies (at least three ≥1 cm in length) increases the yield of diagnosis for benign lesions.

In certain instances, nonradiologic biopsies of pulmonary nodules may provide higher yields than image-guided procedures. Video-assisted thoracoscopic biopsy may have a very high success rate in patients with subpleural nodules, and bronchoscopic biopsy of central intraluminal lesions may also provide better success rates compared to percutaneous biopsy. Although the data are currently sparse, performing molecular analysis on bronchoscopically obtained endobronchial epithelial lining fluid from a subsegmental bronchus close to a pulmonary nodule has shown promise in the early diagnosis of lung cancer. At this time, for peripheral pulmonary nodules, CT-guided biopsies still provide a higher yield than endobronchial US-guided sheath biopsies.

Percutaneous lung biopsy is generally associated with higher complication rates compared to solid organ biopsy. The Society of Interventional Radiology has published guidelines stating that an overall complication rate of 10% is acceptable for lung biopsies, compared to 2% for all other organ systems. The most common complication of percutaneous lung biopsy is bleeding (hemoptysis, chest wall, parenchymal); however, the most common complication requiring intervention is pneumothorax (10% to 30%). Chest tube insertion is needed in approximately one-third of patients with pneumothoraces. Most postbiopsy complications can be treated conservatively, often on an outpatient basis. Some evidence suggests that the use of an autologous intraparenchymal blood patch decreases the rate of pneumothorax requiring chest tube insertion. Embolization of the tract following biopsy using a coaxial system has been described, with embolization agents varying from collagen foam plugs to autologous clot to fibrin glue to normal saline. The risk of chest wall implantation caused by percutaneous biopsy is rare, with reports ranging from 0% to 3%.

Patients who undergo percutaneous lung biopsies that yield a definitive malignant diagnosis may or may not undergo therapy. False-positive results are very rare. Patients with definitive benign diagnoses can be managed conservatively, although false-negative results may occur in a minority of patients. Patients who do not have either a definitive malignant or benign diagnosis need close follow-up, surgical referral, or repeat biopsy (either percutaneous or by other means). Death from percutaneous lung biopsy is extremely rare but may occur from systemic air embolism.

Variants 9 through 11: Mediastinal Nodes and Masses

Mediastinal masses may arise without a concurrent intraparenchymal pulmonary mass and may represent metastatic disease. Definitive diagnosis by biopsy is vital in that it may significantly change the treatment options or may preclude the need for exploratory surgery. The best method of biopsy largely depends on the location of the mass and the proximity of adjacent structures.

Image-guided biopsies of mediastinal masses are almost always performed using CT guidance. The lack of an acoustic window prevents the use of US, unless the mass extends to the pleural surface or invades the chest wall. Real-time CT guidance, however, may be more difficult than expected because of its relatively poor visualization of vascular structures on unenhanced CT. In select instances, the use of iatrogenic saline windows (so-called "salinomas") or artificially-induced pneumothoraces may be helpful in decreasing the incidence of postbiopsy pneumothorax by moving the pleural surface away from the needle path. Several approaches have been described, including parasternal, suprasternal, and even trans-sternal. Awareness of the internal mammary vessels is crucial in safely performing a parasternal approach. Although magnetic resonance imaging (MRI)-guided percutaneous biopsy of mediastinal masses has been proven to be safe and effective, current technology limits its widespread use.

Traditionally, central pulmonary hilar lesions are approached by bronchoscopic biopsy with or without endobronchial US guidance. However, CT-guided biopsy of pulmonary hilar lesions has high sensitivity and accuracy and is a viable alternative for bronchoscopic biopsy, though the procedure can result in high rates of pneumothorax and chest tube insertion.

Nonradiologic mediastinal mass biopsy may be safer and have higher yields compared to radiologic biopsy. Bronchoscopically guided transbronchial FNA, endoscopic transesophageal US with FNA, mediastinoscopy, endobronchial US, and thoracoscopy can all be used to obtain tissue from mediastinal masses. One recent study suggested that endobronchial US-guided transbronchial needle aspiration (TBNA) was preferable as the primary procedure to endoscopic US-guided FNA in the mediastinal staging of lung cancer, although many patients required both examinations to make the definitive diagnosis. The indications for image-guided versus nonradiologic procedures will vary from institution to institution.

Variant 12: Pleural Biopsies

Although malignant processes affecting the pleural surface can sometimes be diagnosed by evaluating pleural fluid on the affected side, the yield of such a procedure is often low. Pleural biopsies can be separated on the basis of whether the region of interest is a focal mass or a diffuse process. Biopsies for diffuse processes, such as tuberculosis, are frequently done without imaging guidance. Biopsies for focal pleural-based mass lesions can frequently be performed with US guidance, particularly in the presence of a pleural effusion; diagnostic yield is essentially the same with US as with CT guidance. Due to the paucity of evidence in the literature, complication rates of pleural mass–based biopsies are impossible to determine; however, it is anticipated that the risk of pneumothorax will be somewhat lower than that demonstrated with intraparenchymal biopsies.

Summary of Recommendations

Intraparenchymal Pulmonary Nodules

- The choice of modalities (percutaneous with imaging guidance, bronchoscopy, video-assisted thoracoscopy, mediastinoscopy, or open surgical) depends in large part on the location and size of the lesion, the underlying pulmonary function, adjacent structures, clinical expertise at the particular practice, and operator preference.
- In patients with incidentally noted pulmonary nodules that do NOT have an appearance typical of malignancy (e.g., nodule has smooth borders and calcification and does not invade surrounding structures) and no known risk factors, conservative follow-up with imaging is more appropriate than biopsy.
- PET imaging is very sensitive for nodules >0.8 mm in diameter; however, there is a relatively high rate of false negatives. PET may be particularly helpful during follow-up of patients postintervention and for assessing patients for distant metastatic disease.
- Increased diagnostic yield is expected when core biopsy is performed in addition to FNA. The greater tissue yield also allows for mutational tumor-specific genetic testing.
- Slide fixation at the time of FNA improves diagnostic yield compared to placing the specimen in a fixative for later cytopathologic evaluation.
- Most complications can be treated using percutaneous techniques, and many can be treated on an outpatient basis.
- Delayed pneumothorax is known to occur but is a rare complication.

Mediastinal Masses/Adenopathy

- In select patient populations, image-guided percutaneous FNA and biopsy may provide the highest diagnostic yield in the safest manner.
- Nonradiologic biopsies (e.g., mediastinoscopy with biopsy, bronchoscopic or endoscopic US-guided transbronchial or transesophageal biopsy) may provide a safer alternative to percutaneous biopsy.

Pleural Biopsies

- Pleural biopsies for diffuse disease (e.g., tuberculosis) can typically be performed without imaging guidance.
- Biopsies of focal pleural masses can be performed safely with either CT or US guidance.

Many of the diagnostic, surgical, and interventional procedures described here are highly specialized. Their availability and utility vary by institutional and operator experience.

Abbreviations

- COPD, chronic obstructive pulmonary disease
- CT, computed tomography
- EBUS, endobronchial ultrasound
- FDG-PET, fluorine-18-2-fluoro-2-deoxy-D-glucose–positron emission tomography
- TBNA, transbronchial needle aspiration

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

- Thoracic nodules and masses
- Lung cancer, including metastatic lung disease

Guideline Category

Diagnosis

Management

Clinical Specialty

Internal Medicine

Oncology

Pulmonary Medicine

Radiology

Thoracic Surgery

Intended Users

Advanced Practice Nurses

Health Plans

Hospitals

Managed Care Organizations

Physician Assistants

Physicians

Students

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of biopsies of thoracic nodules and masses

Target Population

Patients with thoracic nodules or masses and suspected lung cancer or suspected metastatic disease to the lung

Interventions and Practices Considered

1. Percutaneous lung biopsy
2. Surgical lung biopsy/resection
3. Endoscopic/bronchoscopic biopsy
4. Bronchoscopic biopsy (repeat biopsy)
5. Percutaneous mediastinal biopsy
6. Surgical mediastinal biopsy/resection
7. Endoscopic/bronchoscopic mediastinal biopsy
8. Surgical pulmonary nodule biopsy/resection
9. Surgical pleural biopsy/resection
10. Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography (FDG-PET), whole body
11. Conservative management (do nothing)
12. Follow-up imaging only

Major Outcomes Considered

- 5-year survival rate
- Failure rate of lung biopsies
- Utility and diagnostic accuracy of biopsy and positron emission tomography-computed tomography (PET/CT) in differential diagnosis
- Risk factors for and rate of pneumothorax
- Complication rates of biopsy procedures

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Summary

Of the 39 citations in the original bibliography, 28 were retained in the final document. Articles were removed from the original bibliography if they were more than 10 years old and did not contribute to the evidence or they were no longer cited in the revised narrative text.

A new literature search was conducted in December 2013 to identify additional evidence published since the *ACR Appropriateness Criteria® Radiologic Management of Thoracic Nodules and Masses* topic was finalized. Using the search strategy described in the literature search companion (see the "Availability of Companion Documents" field), 231 articles were found. Five articles were added to the bibliography. Two hundred twenty-six articles were not used due to either poor study design, the articles were not relevant or generalizable to the topic, the results were unclear, misinterpreted, or biased, or the articles were already cited in the original bibliography.

The author added 31 citations from bibliographies, Web sites, or books that were not found in the new literature search.

See also the American College of Radiology (ACR) Appropriateness Criteria® literature search process document (see the "Availability of Companion Documents" field) for further information.

Number of Source Documents

Of the 39 citations in the original bibliography, 28 were retained in the final document. The new literature search conducted in December 2013 identified five articles that were added to the bibliography. The author added 31 citations from bibliographies, Web sites, or books that were not found in the new literature search.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions of Study Quality Categories

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - The study has important study design limitations.

Category 4 - The study or source is not useful as primary evidence. The article may not be a clinical study, the study design is invalid, or conclusions are based on expert consensus.

> The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
>
> *Or*
>
> The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
>
> *Or*
>
> The study is an expert opinion or consensus document.

Category M - Meta-analysis studies are not rated for study quality using the study element method because the method is designed to evaluate individual studies only. An "M" for the study quality will indicate that the study quality has not been evaluated for the meta-analysis study.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author assesses the literature then drafts or revises the narrative summarizing the evidence found in the literature. American College of Radiology (ACR) staff drafts an evidence table based on the analysis of the selected literature. These tables rate the study quality for each article included in the narrative.

The expert panel reviews the narrative, evidence table, and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the variant table(s). Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development documents (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The American College of Radiology (ACR) Appropriateness Criteria (AC) methodology is based on the RAND/UCLA Appropriateness Method. The appropriateness ratings for each of the procedures or treatments included in the AC topics are determined using a modified Delphi method. An initial survey is conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. The expert panel members review the evidence presented and assess the risks or harms of doing the procedure balanced with the benefits of performing the procedure. The direct or indirect costs of a procedure are not considered as a risk or harm when determining appropriateness (additional assumptions regarding rating appropriateness can be found in the document Rating Round Information). When the evidence for a specific topic and variant is uncertain or incomplete, expert opinion may supplement the available evidence or may be the sole source for assessing the appropriateness.

The appropriateness is represented on an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate" where the harms of doing the procedure outweigh the benefits; and 7, 8, or 9 are in the category "usually appropriate" where the benefits of doing a procedure outweigh the harms or risks. The middle category, designated "may be appropriate," is represented by 4, 5, or 6 on the scale. The middle category is when the risks and benefits are equivocal or unclear, the dispersion of the individual ratings from the group median rating is too large (i.e., disagreement), the evidence is contradictory or unclear, or there are special circumstances or subpopulations which could influence the risks or benefits that are embedded in the variant.

The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating. To determine the panel's recommendation, the rating category that contains the median group rating without disagreement is selected. This may be determined after either the first or second rating round. If there is disagreement after the first rating round, a conference call is scheduled to discuss the evidence and, if needed, clarify the variant or procedure description. If there is still disagreement after the second rating round, the recommendation is "may be appropriate."

This modified Delphi method enables each panelist to articulate his or her individual interpretations of the evidence or expert opinion without excessive influence from fellow panelists in a simple, standardized, and economical process. For additional information on the ratings process see the Rating Round Information document.

Additional methodology documents, including a more detailed explanation of the complete topic development process and all ACR AC topics can be found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current medical evidence literature and the application of the RAND/UCLA appropriateness method and expert panel consensus.

Summary of Evidence

Of the 64 references cited in the *ACR Appropriateness Criteria® Radiologic Management of Thoracic Nodules and Masses* document, 60 are categorized as diagnostic references including 5 well designed studies, 7 good quality studies, and 27 quality studies that may have design limitations. Additionally, 4 references are categorized as therapeutic references including 1 good quality study. There are 24 references that may not be useful as primary evidence.

While there are references that report on studies with design limitations, 13 well designed or good quality studies provide good evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- The diagnosis of lung cancer carries a very poor prognosis; the expected 5-year survival rate for all patients in whom lung cancer is diagnosed is 15.5% (compared to 64.8% for colon cancer, 89% for breast cancer, and 99.9% for prostate cancer). Early diagnosis is vital and significantly improves survival rates.
- Metastatic disease to the lungs can occur with virtually any primary malignancy. Diagnosis of such metastases allows for appropriate treatment and prognostication of patients with the disease.
- Biopsy of pulmonary nodules allows for a tissue diagnosis of malignancy and, in some cases, staging of the primary tumor. Diagnosis by less invasive means may also preclude more invasive surgical procedures performed for diagnosis; this is particularly important in this high-risk patient population. For example, findings from positron emission tomography/computed tomography (PET/CT) have been shown to reduce the number of futile thoracotomies and the total number of thoracotomies.
- The National Lung Cancer Screening Trial demonstrated that, when compared to chest radiography, screening with low-dose CT resulted in a decrease in the number of advanced-stage lung cancers while concurrently resulting in an increase in the number of early lung cancers. There was a 20% reduction in lung cancer mortality from the low-dose CT screening arm compared to chest radiography screening, and there was a 7% reduction in all-cause mortality.

Potential Harms

- Although studies have demonstrated the ability of low-dose computed tomography (CT) to identify early-stage malignancy in high-risk patients, concern has been raised about both the radiation exposure to the public with aggressive and widespread screening protocols as well as the low yield of screening protocols. In 1 large study from Italy (ITALUNG), a yield of only 2.0% for malignancy was noted in patients exposed to up to 4 annual screening CT scans.
- Fluorine-18-2-fluoro-2-deoxy-D-glucose–positron emission tomography (FDG-PET) is best used in patients with nodules >0.8 mm in diameter, as smaller nodules may result in a false-negative study. False-negative scans may also occur in cancer presenting as a predominant ground-glass opacity and with malignancies such as well-differentiated adenocarcinomas, bronchoalveolar cell carcinomas, and carcinoid tumors. False-positive lesions may result in patients with tuberculosis, fungal infections, or sarcoidosis.
- Percutaneous lung biopsy is generally associated with higher complication rates compared to solid organ biopsy. The Society of Interventional Radiology has published guidelines stating that an overall complication rate of 10% is acceptable for lung biopsies, compared to 2% for all other organ systems. The most common complication of percutaneous lung biopsy is bleeding (hemoptysis, chest wall, parenchymal); however, the most common complication requiring intervention is pneumothorax (10% to 30%). Chest tube insertion is needed in approximately one-third of those with pneumothoraces. Most postbiopsy complications can be treated conservatively, often on an outpatient basis. Some evidence suggests that the use of an autologous intraparenchymal blood patch decreases the rate of pneumothorax requiring chest tube insertion. Embolization of the tract following biopsy using a coaxial system has been described, with embolization agents varying from collagen foam plugs to autologous clot to fibrin glue to normal saline. The risk of chest wall implantation caused by percutaneous biopsy is rare, with reports ranging from 0% to 3%. False-positive results occur very rarely; false-negative results may occur in a minority of patients. Death from percutaneous lung biopsy is extremely rare but may occur from systemic air embolism.
- Patients in whom biopsies are performed are often considered to be at high risk for complications from the procedure. These risks (e.g.,

pneumothorax, bleeding, and bronchopleural fistula) are largely due to the poor underlying pulmonary reserve and high incidence of chronic obstructive pulmonary disease (COPD) in this patient population. Patients should be counseled before the procedure regarding the significant risks associated with their biopsy. In addition to problems associated with a relatively high-risk patient population, percutaneous biopsies of pulmonary nodules may be difficult to perform technically. Patients may often have difficulty suspending respirations or may take variable volume breaths, resulting in the target lesion moving in and out of the biopsy plane. Lesions may also be very small or central (deep) in location, making needle placement challenging. For these reasons and others, the failure rate of lung biopsies is relatively high.

- CT-guided biopsy of pulmonary hilar lesions can result in high rates of pneumothorax and chest tube insertion.
- Due to the paucity of evidence on pleural biopsy in the literature, complication rates of pleural mass–based biopsies are impossible to determine; however, it is anticipated that the risk of pneumothorax will be somewhat lower than that demonstrated with intraparenchymal biopsies.

Qualifying Statements

Qualifying Statements

- The American College of Radiology (ACR) Committee on Appropriateness Criteria (AC) and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.
- ACR seeks and encourages collaboration with other organizations on the development of the ACR AC through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply individual or society endorsement of the final document.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

English BS, Ray CE Jr, Chang JY, Crabtree TD, Gaba RC, Gipson MG, Iannettoni MD, Kouri BE, Marshalleck FE, Mohammed TL, Pinchot JW, Saleh AG, Willers H, Hohenwalter EJ, Expert Panel on Interventional Radiology. ACR Appropriateness CriteriaÂ® radiologic management of thoracic nodules and masses. Reston (VA): American College of Radiology (ACR); 2015. 14 p. [64 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

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The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Interventional Radiology

Composition of Group That Authored the Guideline

Panel Members: Benjamin S. English, MD (*Research Author*); Charles E. Ray, Jr, MD, PhD (*Principal Author and Specialty Chair*); Joe Yujiao Chang, MD, PhD; Traves D. Crabtree, MD; Ron C. Gaba, MD; Matthew G. Gipson, MD; Mark D. Iannettoni, MD; Brian E. Kouri, MD; Francis E. Marshalleck, MBBS; Tan-Lucien H. Mohammed, MD; Jason W. Pinchot, MD; Anthony G. Saleh, MD; Henning Willers, MD; Eric J. Hohenwalter, MD (*Panel Chair*)

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Ray CE Jr, English B, Funaki BS, Burke CT, Fidelman N, Ginsburg ME, Kinney TB, Kostelic JK, Kouri BE, Lorenz JM, Nair AV, Nemcek AA Jr, Owens CA, Saleh AG, Vatakencherry G, Mohammed TH, Expert Panel on Interventional Radiology. ACR Appropriateness Criteria® radiologic management of thoracic nodules and masses. [online publication]. Reston (VA): American College of Radiology (ACR); 2011. 7 p. [39 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the American College of Radiology (ACR) Web site .

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2015 Oct. 3 p. Available from the American College of Radiology (ACR) Web site .
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2015 Feb. 1 p. Available in from the ACR Web site .
- ACR Appropriateness Criteria®. Evidence table development. Reston (VA): American College of Radiology; 2015 Nov. 5 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Topic development process. Reston (VA): American College of Radiology; 2015 Nov. 2 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Rating round information. Reston (VA): American College of Radiology; 2015 Apr. 5 p. Available from the ACR Web site .
- ACR Appropriateness Criteria® radiologic management of thoracic nodules and masses. Evidence table. Reston (VA): American College of Radiology; 2015. 23 p. Available from the ACR Web site .
- ACR Appropriateness Criteria® radiologic management of thoracic nodules and masses. Literature search. Reston (VA): American College of Radiology; 2015. 1 p. Available from the ACR Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on March 28, 2002. The information was verified by the guideline developer on May 28, 2002. This summary was updated by ECRI Institute on June 25, 2009. This summary was updated by ECRI Institute on July 6, 2011. This summary was updated by ECRI Institute on January 20, 2016.

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